

Docket No. 2081-0125P

## REMARKS

The helpfulness and courtesies extended by the Examiner to Applicant's representatives during the interview of 22 June 2004 are sincerely appreciated. The Interview Summary Record of that date fairly summarizes the discussions during the interview.

New claims 71 and 72 discussed during the interview have been added to the application. Those claims find support in the original claims, such as claim 48, and in the specification at, for example, pages 18-19; page 15, lines 20 - 32 and page 16, lines 17 -19. As discussed during the interview, as compared to claim 57, claims 71 and 72 more specifically define the groups  $R^1$ ,  $R^2$  and  $R^3$ .

During the interview, Applicant's representatives discussed the principles behind the functioning of the present invention, including the avoidance of severe hemolysis and death which would occur by direct injection of anticancer ether lipid drugs (AELs) which concerns are overcome in the present invention by producing a pro-AEL construct which forms pro-AEL lipid bilayers which when injected into a patient are preferentially directed to the tumors wherein high concentrations of extracellular PLA2 cause a release of the active AEL. In this manner, the present invention provides tumor specific delivery of AELs while avoiding toxic side effects which would otherwise be encountered by direct administration of AEL. Enclosed as Exhibit A are

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several pages of schematic representations of these principles of the present invention.

In view of the above, taken together with Applicants previously submitted preliminary amendment and arguments, Applicants submit that the present claims define a patentable invention over the prior art. Favorable action on the application is, therefore, requested.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By 

Leonard R. Svensson, #30,330

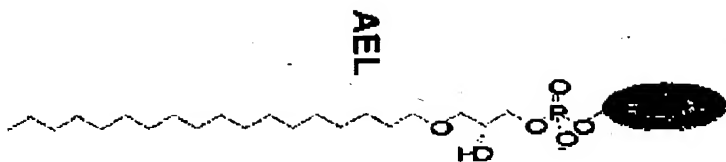
LRS/lmt  
2081-0125P

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Attachment(s): Exhibit A

**EXHIBIT A**

# Liposomal prodrug principle – activation of AELs in tumor tissue by PLA2



**i.v. injection of  
AEIs causes  
severe hemolysis  
and death**

## Tumor

### i. v. injection of proAEL

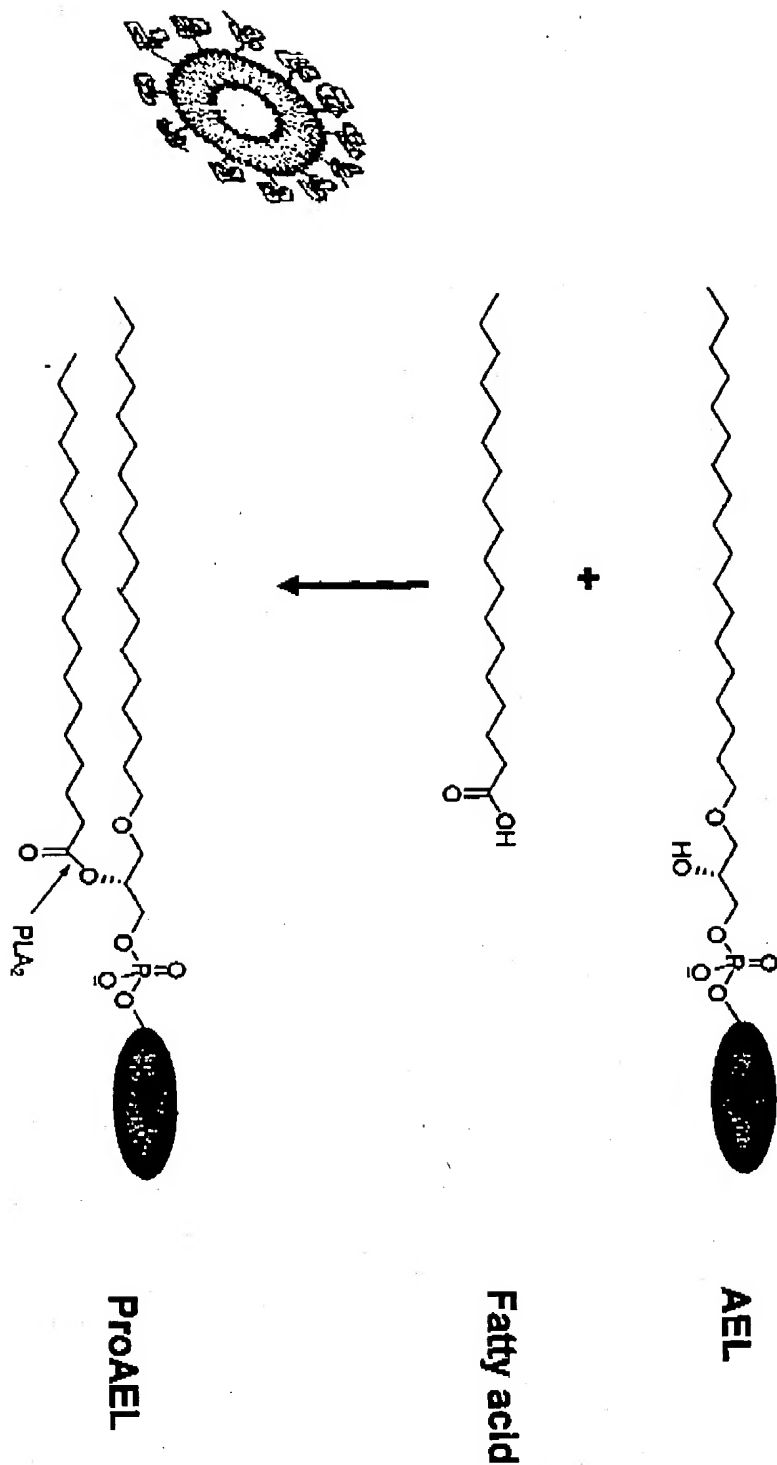
**no hemolysis**

**proAEL lipid  
bilayers form  
liposomes**

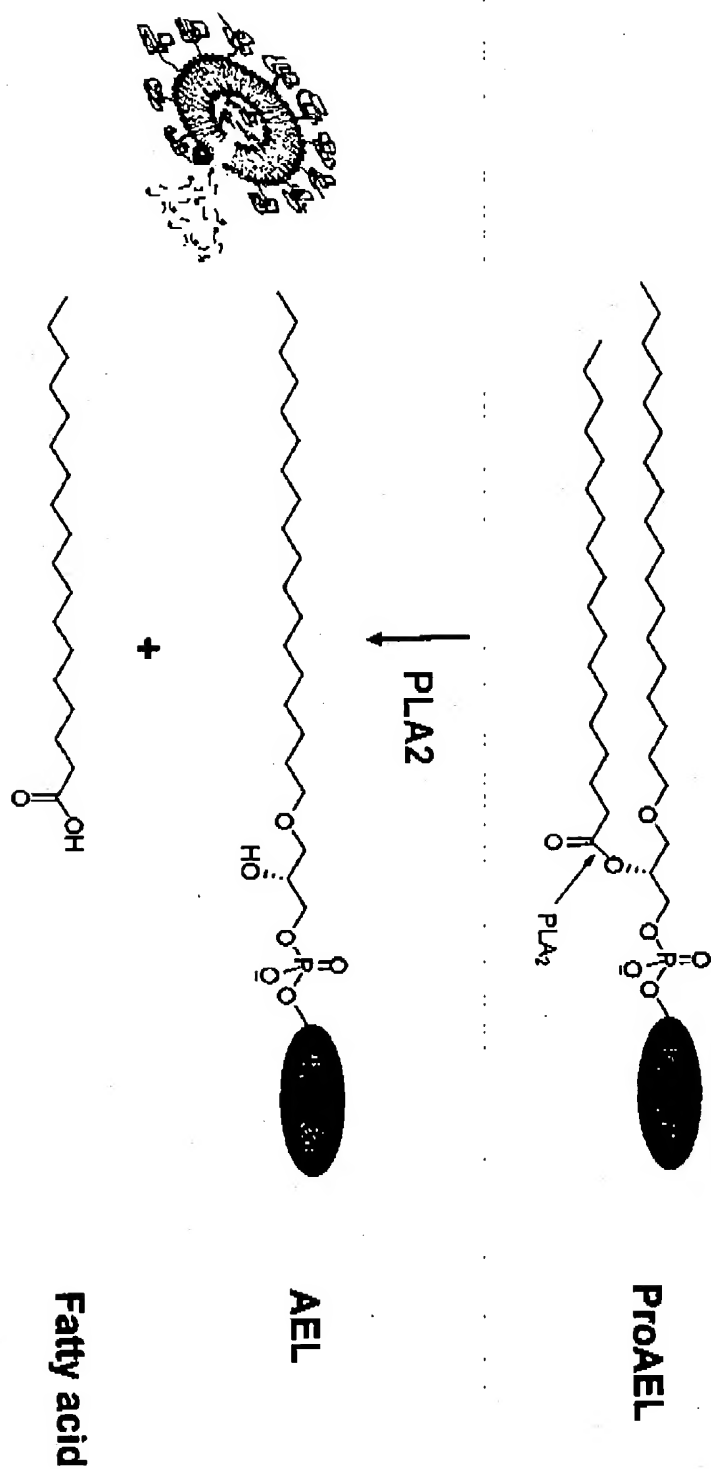
**proAELs form  
lipid bilayers**

anticancer lipid (AEL)  
prodrug of anticancer lipid (proAEL)  
extracellular phospholipase A2 (PLA2)

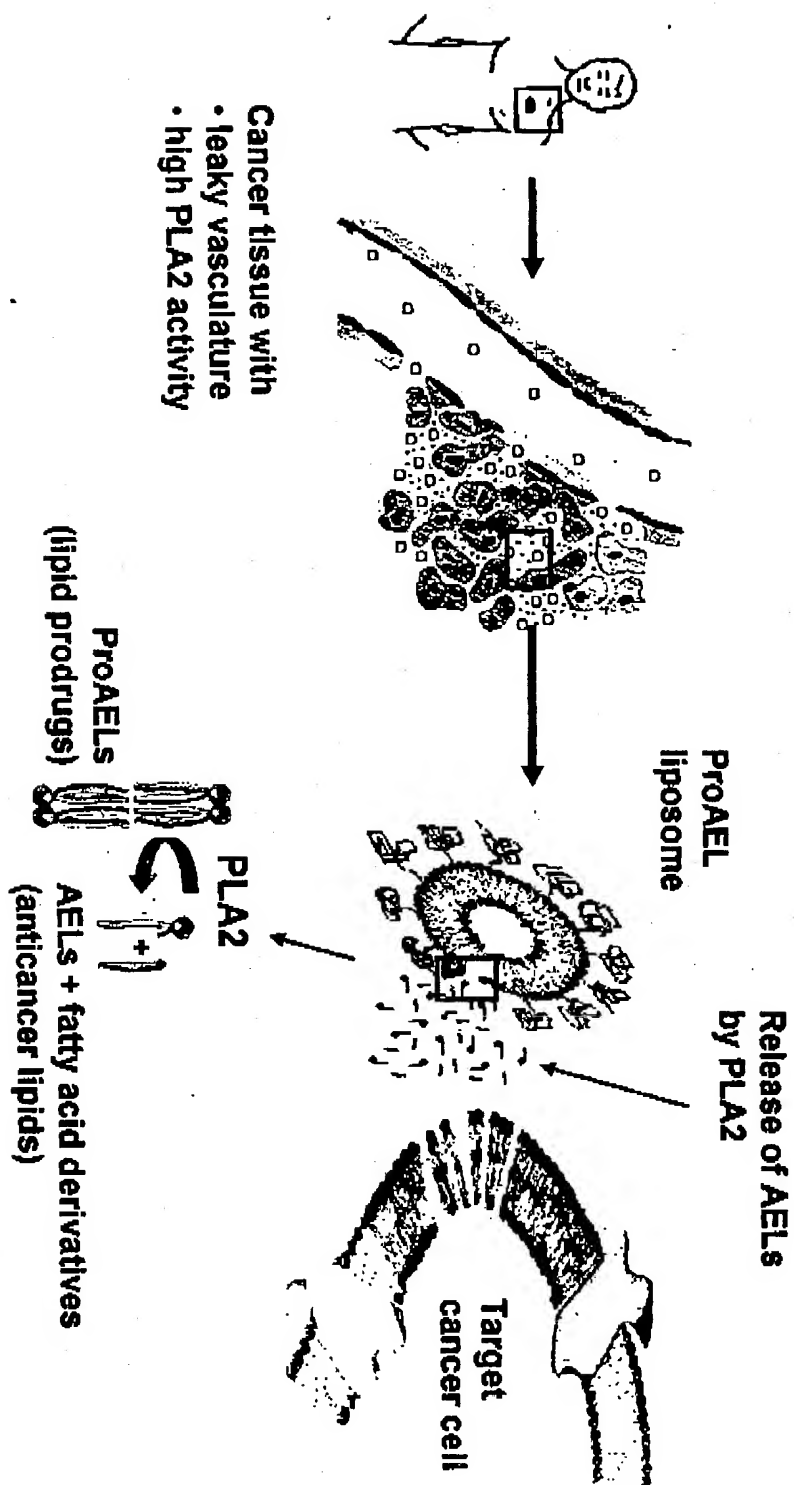
# AEL + fatty acid = proAEL lipid



## PLA2 triggers AEL release in tumor tissue



# Tumor specific delivery of AEIs by PLA2



# Tumor specific delivery of AELs by PLA2

